UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/634,320	08/09/2000	Mikhail I. Papisov	0838.1003-001	5525

21005 7590 10/04/2002

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.
530 VIRGINIA ROAD
P.O. BOX 9133
CONCORD, MA 01742-9133

EXAMINER	
ZARA, JANE J	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 10/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/634,320	PAPISOV, MIKHAIL I.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-96* is/are pending in the application.

4a) Of the above claim(s) *1-13,18,23-27,31-33 and 35-96* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-17,19-22,28-30 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3 & 8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This communication is in response to the communication filed July 5, 2002, Paper No. 13.

Claims 1-96 are pending in the instant application.

Election/Restriction

Claims 1-13, 18, 23-27, 31-33, 35-96 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 13.

Applicant's election without traverse of Group II in Paper No. 13 is acknowledged.

Claims 14-17, 19-22, 28-30 and 34, drawn to drug carrier compositions comprising a nucleic acid component, a polyacetal polymer component, and which drug is a an intercalating agent, have been examined on the merits as indicated below.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16, 19, 22, 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 16, it is unclear what the polymer component is cross-linked to (i.e. is it cross-linked intramolecularly, or intermolecularly to the nucleotide component of the drug carrier complex?). Appropriate clarification is required.

In claim 19, line 3, the metes and bounds of "derivatives thereof" are unclear. (Does derivatives therof refer to the polyacetal of line 1 or poly(hydroxymethylethylene hydroxymethylformal) of line 2? Appropriate clarification is reqired.

In claim 22, the metes and bounds of "chemically distinct polymers" cannot be determined. Appropriate clarification is required.

In claim 34, line 3, the claim appears grammatically incorrect (i.e. it is unclear in line b, should it be "polymers which are"?). Appropriate corrected is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19 and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a drug carrier comprising a polymer component and a nucleotide component, which polymer component comprises a polyacetal selected from the group consisting

of poly(hydroxymethylethylene hydroxymethylformal) and derivatives thereof, or which polyacetal component includes at least two chemically distinct polymers.

The specification and claims do not describe elements which are essential to the genera comprising chemically distinct polyacetal polymers, or comprising derivatives of the polyacetal polymer poly(hydroxymethylethylene hydroxymethylformal). The disclosure does not clarify what common attributes are encompassed by these genera. The scope of the claims includes numerous structural variants, and the genera are highly variant because a significant number of structural differences between members of these genera is permitted. Concise structural features that could distinguish structures or compounds within the genera from others are missing from the disclosure. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general guidance is what is needed. The specification fails to teach or adequately describe a representative number of species in each genera such that the common attributes or characteristics concisely identifying members of each proposed genera are exemplified, and because each genus is highly variant, the description provided in insufficient. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genera claimed. Thus, Applicant was not in possession of the claimed genera.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 28, 30 and 34 are rejected under 35 U.S.C. 102(a) or (e) as being anticipated by Burke et al.

Burke et al teach diagnostic, therapeutic or prophylactic drug carrier compositions comprising a biocompatible, polyacetal polymeric component, and comprising double stranded or single stranded polynuceotides, and which polymer component is optionally heterogenous or homogenous (i.e. optionally comprising at least two chemically distinct polymers), which drug carrier complex comprises reversible associations (i.e. salt or ionic bridges, hydrogen bonding)

between the polymer, nucleic acid and drug components (See entire document, especially col. 2, line 44- col. 5, line 11; col. 6, line 64- col. 7, line 16; claims 3 and 11).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 14-17, 20-22, 28-30 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burke et al as applied to claims 28, 30 and 34 above, and further in view of the combination of Matysiak et al, Ishihara et al and Gao et al.

The claims are drawn to drug carrier compositions comprising a nucleotide component, a biocompatible polyacetal polymer component or derivative thereof and a drug which comprises an intercalating agent, whereby the polymer and the nucleic acid components are optionally covalently crosslinked, or whereby the polymer, drug and nucleic acid components are reversibly associated, and which polymer component has an aqueous solubility of at least one mg/liter at 25°C.

Burke et al is relied upon as cited in the 102 rejection above.

Burke et al does not teach covalent linkages between the polyacetal and the nucleotide components, nor drug carrier compositions comprising intercalating agents.

Matysiak et al teaches bioconjugates comprising covalent conjugation or crosslinking of oligonucleotides to other molecules utilizing acetal moieties and derivatives thereof, and which polymer component has an aqueous solubility of at least one mg/liter at 25°C (see entire document, especially figures 2 and 3 on pages 856-857, and the text on pages 857-860).

Ishihara et al teaches drug carriers comprising nucleotide components and intercalating agents, which are optionally covalently conjugated or alternatively linked via reversible associations, including ionic complexes (see especially col. 1, lines 24-55).

Gao et al teaches the use of intercalating agents as anticancer drugs, whereby the bis intercalating agent, ditercalinium, induced DNA repair in target cells (See especially 2422 and first paragraph of the discussion on bottom of page 2424- top of page 2425).

It would have been obvious to one of ordinary skill in the art to design and utilize drug carriers comprising a nucleotide component and a biocompatible polyacetal component because such drug carrier complexes have been successfully designed and utilized for target cell delivery of various agents including for labile drug delivery, as taught previously by Burke et al. One of ordinary skill in the art would have been motivated to utilize such drug carriers for target cell delivery of therapeutic or diagnostic agents because these biocompatible complexes have been shown by Burke et al to enhance delivery of labile drugs to target cells upon administration to an organism compared to drugs administered without protective carrier complexes, providing

increased quantities of drugs to the target cell in a biologically active form. One of ordinary skill in the art would have expected that biologically compatible nucleotide conjugates are obtained utilizing acetal containing polymers because nucleotide conjugation to various moieties utilizing acetal groups have been taught previously by Matysiak et al, and covalently linked nucleotide conjugates have been shown to have enhanced biological stability in appropriate biological contexts compared to non-conjugated drug carriers, as taught previously by Ishihara et al. One of ordinary skill in the art would have been motivated to utilize polyacetals in generating nucleotide containing bioconjugates or drug carriers because conjugates containing variying stoichiometries of conjugate components are generated utilizing polyacetal groups, allowing flexibility to optimize for best stoichiometries for a particular drug carrier complex in order to achieve a desired biological effect. One of ordinary skill in the art would have been motivated to utilize intercalating agents for therapeutic or diagnostic purposes because intercalating agents are known to be successfully delivered to target cells as bioconjugates, as taught previously by Ishihara et al, where the intercalators insert themselves into double stranded DNA, and intercalating agents have been used historically to generate mutations in the DNA of target cells or alternatively for detection or diagnostic purposes, once delivered to a target cell. In addition, the bis-intercalating agent, ditercalinium has been used as an anticancer drug by inducing DNA repair systems when delivered to target cells, as taught previously by Gao et al.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(703) 306-5820.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

KAREN LACOURCIERE
PATENT EXAMINER

JZ

October 1, 2002